ABSTRACT
Hydrogen sulfide is a potent lethal gas. Supportive care, nitrite therapy and hyperbaric oxygen are the treatment modalities reported in the literature in cases of hydrogen sulfide exposure. We describe an industrial exposure in which 6 workers inhaled high concentrations of hydrogen sulfide when they entered a closed spreader tank partially filled with liquid swine manure. Five of the 6 lost consciousness, and 2 were agitated and poorly responsive on arrival to the emergency department despite having already received high-flow oxygen for nearly 1 hour. These 2 patients received nitrite therapy followed by orotracheal intubation and hyperbaric oxygen. All patients were discharged home without sequelae after short stays in hospital. The emergency management of hydrogen sulfide exposure is briefly reviewed.

Key words: hyperbaric oxygen therapy; hydrogen sulfide; liquid swine manure; nitrite therapy

TOXICOLOGY • TOXICOLOGIE

Hyperbaric oxygen therapy in the management of two cases of hydrogen sulfide toxicity from liquid manure

Richard Belley, MD, CFPC; Nicolas Bernard, MD; Mario Côté, MD; Francois Paquet, MD, CSPQ; Julien Poitras, MD, CSPQ

Introduction
Hydrogen sulfide is a colourless gas that has been recognized as an occupational hazard for at least 2 centuries. It has been referred to as the “knock down gas” because inhalation of high concentrations can cause immediate loss of consciousness and death. Hydrogen sulfide is found in significant concentration in livestock wastes kept in large tanks in the farming industry. Up to 5% of patients with hydrogen sulfide intoxication die at the scene. Those who survive to reach the emergency department (ED) typically present with coma, neurological symptoms and respiratory
distress from pulmonary edema. Long-term neurological and neuropsychiatric sequela have been reported, as well as delayed neuropsychiatric symptoms up to 5 years post-exposure. Supportive care, nitrite administration and hyperbaric oxygen therapy are the treatment options reported in the literature, although hyperbaric oxygen remains controversial because of the lack of good clinical studies.

Case report

Six workers were exposed to gas from liquid swine manure stocked in a spreader tank. Without using any protective or respiratory apparatus, they attempted to repair a defective valve inside the tank, which contained 4 to 5 inches of liquid swine manure. Patient 1, a 48-year-old male, was the first to enter the tank; he rapidly lost consciousness. Patient 2, a 16-year-old male, entered the tank in an attempt to rescue Patient 1 and rapidly lost consciousness as well. Their length of stay in the tank is estimated to be 30 to 40 minutes. Paramedics reported that Patient 1 had seizures lasting 2 to 3 minutes as he was being extricated from the tank. All patients were decontaminated on site, received 100% oxygen by non-rebreather mask and were transferred to our ED. The interval from rescue to ED arrival was approximately 50 minutes.

Investigators subsequently failed to detect hydrogen sulfide in the tank on site; however, their measurements were made using a probeless 4-gas analyzer held over the top opening after the tank had been vented (the gas analyzer was later found to be defective). A simulation reproducing the circumstances of the accident suggested that the likely gas concentrations in the tank were as follows: 440 parts per million (ppm) of hydrogen sulfide, 13 600 ppm of carbon dioxide, more than 50 ppm ammonia, 3300 ppm of methane, 1.5 ppm of carbon monoxide and 20.2% oxygen.

Patient 1

On arrival in the ED, the patient was anxious and agitated with abnormal vital signs and lab values (Table 1). Inhaled amyl nitrite 0.3 mg was administered within 10 minutes of the patient’s arrival, followed by intravenous (IV) sodium nitrite, 300 mg. He became poorly responsive, and his vital signs deteriorated; therefore he was intubated using a rapid sequence technique. His ECG and cerebral computed tomography (CT) were normal, and the chest x-ray demonstrated an alveolar infiltrate in the right upper lobe. Intra-venous methylprednisolone 125 mg was administered, and he was moved to our Perry Sigma Dualplace Hyperbaric System chamber (Perry Baromedical Corporation, Riviera Beach, Fla.). Three hyperbaric oxygen (HBO) treatments were administered at 6, 12 and 22 hours post arrival. Each treatment consisted of 100% oxygen for 90 minutes. Treatments were conducted under sedation and neuromuscular blockade, the first at 2.8 absolute atmospheres and subsequent treatments at 2.4 absolute atmospheres.

The chest x-ray normalized within 24 hours, and the patient was extubated at 72 hours. He was discharged from hospital 4 days post-extubation with residual short-term retrograde amnesia; however, the patient and his relatives felt his memory function had returned to normal. At 2-month follow-up, he felt well but described headaches and dizziness that persisted 48 hours after hospital discharge, as well as tiredness and lassitude that lasted a week. He still complained of short-term memory problems that did not affect his day-to-day life. His Mini-Mental Status Exam score was 29/30. No other abnormalities were noted in the history and physical exam. Full neuropsychiatric testing was not done.

Patient 2

In the field, paramedics documented significant hypotension (80/60 mm Hg), but this resolved prior to ED arrival (Table 1). Upon arrival, inhaled amyl nitrite 0.3 mg was administered, followed by sodium nitrite 300 mg IV. The patient became less responsive and lost airway protection, so he was intubated using a rapid sequence technique. Results of an ECG and cerebral CT were normal. The chest CT demonstrated severe diffuse alveolar infiltrates of the right lung and minor alveolar infiltrates of the left lung. Methylprednisolone 125 mg IV, clindamycin 900 mg IV, and ciprofloxacin 400 mg IV were given, and HBO therapy was administered at 4, 17 and 25 hours post-arrival, following the same protocol described for Patient 1. This patient’s troponin I level was slightly increased at 5 hours post admission but normalized within 48 hours and there were no ECG changes during the hospital stay. The chest x-ray normalized within 48 hours, the patient was extubated prior to the last hyperbaric treatment, and he was discharged home 2 days post exposure.

At 2-month follow up, the patient felt well and had resumed school without apparent cognitive sequela, although he stated he had been tired, with headaches and concentration problems that prohibited him from attending school for at least 2 weeks following the event. Follow-up physical exam was normal, as were chest x-ray and respiratory function tests, and he scored 30/30 on the Mini-Mental Status Exam. Full neuropsychiatric testing was not done.

Patients 3 to 6 had less severe exposures, although 3 of them also lost consciousness in the tank. All were alert
Discussion

Fermentation of liquid manure produces about 150 different gases, including hydrogen sulphide, carbon monoxide, methane and ammonia. Carbon monoxide and methane can also cause loss of consciousness but, based on their low concentrations during the incident simulation, we believe they did not contribute significantly to the morbidity described in these case reports. Hypoxemia is another possible cause of coma, but is less likely since measured \( P_{O_2} \) levels were normal during the simulation. Ammonia has a powerful irritant effect that discourages patients from staying in contact with it long enough to lose consciousness. At levels of 700–1000 ppm, hydrogen sulfide causes coma, convulsions and, potentially, cardiorespiratory arrest.

Table 1. Description of vital signs and laboratory values for Patients 1 and 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal values</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vital signs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure, mm HG</td>
<td>162/65</td>
<td>104/70</td>
<td></td>
</tr>
<tr>
<td>Temperature (rectal), °C</td>
<td>37.5</td>
<td>37.8</td>
<td></td>
</tr>
<tr>
<td>Respiration rate, breaths/min</td>
<td>24</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>110</td>
<td>104</td>
<td></td>
</tr>
<tr>
<td>Oxygen saturation, %</td>
<td>100†</td>
<td>93†</td>
<td></td>
</tr>
<tr>
<td><strong>Lab results</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial blood gas ‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.35–7.45</td>
<td>7.37</td>
<td>7.27</td>
</tr>
<tr>
<td>( P_{O_2} ), mm Hg</td>
<td>70–110</td>
<td>175</td>
<td>114</td>
</tr>
<tr>
<td>( PCO_2 ), mm Hg</td>
<td>35–48</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>HCO(_3^–), mmol/L</td>
<td>22–26</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Blood glucose, mmol/L</td>
<td>3.6–11.0</td>
<td>11.0</td>
<td>11.4</td>
</tr>
<tr>
<td>CPK, µmol/L</td>
<td>0–195</td>
<td>134</td>
<td>355</td>
</tr>
<tr>
<td>Troponine I, µg/L</td>
<td>&lt;0.5</td>
<td>0.02</td>
<td>1.52</td>
</tr>
<tr>
<td>BUN, mmol/L</td>
<td>2.5–8.5</td>
<td>7.0</td>
<td>11.4</td>
</tr>
<tr>
<td>Blood creatinine, µmol/L</td>
<td>57–108</td>
<td>111</td>
<td>93</td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>135–147</td>
<td>143</td>
<td>141</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>3.5–5.3</td>
<td>3.6</td>
<td>3.3</td>
</tr>
<tr>
<td>Chloride, mmol/L</td>
<td>98–109</td>
<td>102</td>
<td>100</td>
</tr>
<tr>
<td>AST, µ/L</td>
<td>0–40</td>
<td>n/a</td>
<td>63</td>
</tr>
<tr>
<td>ALT, µ/L</td>
<td>0–45</td>
<td>n/a</td>
<td>54</td>
</tr>
<tr>
<td>Carboxyhemoglobin, %</td>
<td>&lt;3</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Lactate, mmol/L</td>
<td>0.6–2.4</td>
<td>2.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Sulfhemoglobin</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Methemoglobin, %</td>
<td>0–3</td>
<td>0.9</td>
<td>1.5</td>
</tr>
</tbody>
</table>

\( ALT = \) alanine aminotransferase (SGPT); \( AST = \) aspartate aminotransferase (SGOT); \( BUN = \) blood urea nitrogen; \( CPK = \) creatine phosphokinase; \( HCO_3^- = \) bicarbonate; \( PCO_2 = \) partial pressure of carbon dioxide; \( pH = \) hydrogen ion concentration; \( P_{O_2} = \) partial pressure of oxygen

† Vital signs taken on arrival in the emergency department (ED).
‡ Oxygen saturation with 100% inspired oxygen with non-rebreather mask.
§ Arterial blood gas done after intubation with 100% inspired oxygen with an ABL 730 (Radiometer Copenhagen, Denmark).
∥ Lactate, troponine I and methemoglobinemia taken 5 hours post arrival in the ED. Other lab values at arrival in the ED.
lation suggested levels of ~440 ppm, but estimates ranged from 77 to 2200 ppm depending on a number of factors. In addition, actual H$_2$S concentrations in the spreader tank could have reached higher levels due to manure agitation by the workers themselves.

Pathophysiology

Hydrogen sulfide is absorbed through the lungs and causes toxic effects by binding cytochrome oxidase aa3, inhibiting oxidative phosphorylation and inducing cellular anoxia. It is metabolized by oxidation, methylation and metalloprotein reactions, and it is rapidly detoxified to sulfate and thiosulfate by an oxyhaemoglobin-catalyzed reaction.

Organs with exposed membrane surface and those with high oxygen demands — notably the brain, lungs and heart — are most susceptible to injury. Brain damage from hydrogen sulfide poisoning is secondary to cerebral edema and ischemic injury, mostly to the brain stem, basal ganglia, hippocampus and vestibular apparatus. Lung injury results from alteration of pulmonary surfactant, impaired bacterial defences, and mucosal edema. Both patients described in this report demonstrated alveolar infiltrates initially thought to be infectious or inflammatory, but their rapid resolution suggested an inflammatory origin; hence the final diagnosis of inhalation alveolitis. Patient 2 had a borderline troponin elevation without ECG changes, suggesting minimal myocardial toxicity. Myocarditis has previously been documented as the cause of death in a post-mortem examination of a patient who inhaled hydrogen sulfide.

Treatment

After rapid extrication from the site of hydrogen sulfide exposure, therapeutic goals are to inhibit sulfide binding to cytochrome oxidase and to promote sulfide detoxification. Amyl nitrite and sodium nitrite induce methemoglobin, which combines with hydrogen sulfide to form sulfmethemoglobin, a less toxic substance that competes with and displaces H$_2$S from its cytochrome oxidase binding sites. These postulated effects — rapid detoxification of hydrogen sulfide in the blood and reactivation of cytochrome oxidase — are potentially life-saving; therefore nitrite therapy should be initiated as soon as possible.1,14–17 Adverse effects of nitrite therapy include hypotension, vomiting, headache and interference with hemoglobin–oxygen dissociation due to excessive methemoglobin formation. Both patients described here deteriorated after nitrite administration, illustrating the potential hazards of this widely recommended therapy.

Oxygen competes with hydrogen sulfide in binding to cytochrome oxidase, and also enhances sulfide detoxification by oxidizing sulfide to sulfate and thiosulfate.9,18 This suggests a role for hyperbaric oxygen therapy in hydrogen sulfide exposures, although it is not clear whether hyperbaric oxygen enhances the dissociation of the hydrogen sulfide-cytochrome aa3 complex.16–19 In addition to the potentially beneficial effects described above, hyperbaric oxygen therapy triggers peripheral vasoconstriction, reduces cerebral edema, increases tissue oxygen tension, decreases leukocyte adhesion (thus inhibiting inflammatory responses), enhances nerve cell regeneration, and decreases lipid peroxidation.20–22 In severe cases, it is probably best to administer hyperbaric oxygen therapy as early as possible. Hyperbaric oxygen also has reported toxicity, including barotrauma, oxygen toxicity and the risks of transferring an unstable patient to a remote hyperbaric facility.

The hyperbaric treatment protocols applied in these cases were based on a previous hydrogen sulfide case report7 and on the Weaver protocol for carbon monoxide intoxication,23 although CO and H$_2$S have different mechanisms of toxicity. Case reports describing HBO therapy for hydrogen sulfide poisoning are scarce,24–28 and all but one29 favour this modality when initiated early. There are no human clinical trial data available, and it is unlikely that that clinical trials will be conducted in the future. However, in rat models of sulfide poisoning, 3 atmosphere absolute (ATA) oxygen therapy and sodium nitrite administration were associated with lower mortality than 100% oxygen at 1ATAor sodium nitrite alone.30

Conclusion

These cases suggest that hyperbaric oxygen therapy is safe when applied early in patients with severe hydrogen sulfide exposure. It is impossible to know whether our patients’ favourable outcomes were the result of HBO treatment; however, based on these cases and previous data, we believe that, in addition to supportive care and nitrite administration, hyperbaric oxygen therapy, if available, may be considered as early as possible in cases of moderate to severe hydrogen sulfide poisoning.

Competing interests: None declared.

References

2. Burnett WW, King EG, Grace M, Hall WF. Hydrogen sulphide


Correspondence to: Dr. Richard Belley, Emergency Department and Hyperbaric Facility, Centre Hospitalier Affilié de l’Hôtel Dieu de Lévis, 143 rue Wolfe, Lévis QC G6V3Z1